Claims

1.A method for producing cross-linked polysaccharide-protein bio-composites, comprising the type of:

(a) preparing a mixture of the polysaccharide solution and protein solution, the weight ratio of polysaccharide and protein is in a range of 20/80 to 80/20.

(b) adjusting the pH value between 3 and 11 by acid and hydroxyl compound.

(c) processing the cross-linking reaction in the water/organic solution that contains the cross-linked reagent.

2. The method of claim 1, wherein said step (a) the polysaccharide is chosen from the group consisting of hyaluronic acid, carboxymethyl cellulose, pectin, starch, chondroitin-4-sulfate, chondroitin-6-sulfate, alginate, chitosan, agar, carragenan and guar gum.

3. The method claim 1, wherein said step (a) the protein solution is chosen from the group consisting of collagen, gelatin, or the mixture of both.

4. The method claim 1, wherein said step (b) the acid compound chosen from the group consisting of acetic acid, hydrogen chloride, or the mixture of acetic acid and hydrogen chloride.

5. The method claim 1, wherein said step (b) the hydroxyl compound is the hydroxyl group donor of alkalinity, the optimal choice is from the group consisting of sodium hydroxide, potassium hydroxide, or the mixture of both.

6. The method claim 1, wherein said the protein solution is that collagen is dissolved at pH 3 solution, while the solution is made of polysaccharide solution.

7. The method claim 1, wherein said the protein solution is that collagen is dissolved in alkaline solution, while the polysaccharide is dissolved in acid solution, the pH range is between 5 to 11 after mixing the both solutions.

8. The method claim 1, wherein said the protein solution is that collagen is dissolved in acid solution, while the polysaccharide is dissolved in alkaline solution, the pH range is between 5 to 11 after mixing the both solutions.

9. The method claim 1, wherein said the protein solution is that gelatin is dissolved in de-ionized water, and the ion strength is adjusted by sodium chloride.

10.The method claim 1, wherein said step (b) the mixture solution is adjusted by acid and hydroxyl compound, and allow to spread to yield a film after degas, or cast into a mold and freeze-dry to yield a proposity matrix, or emulsify to yield a powder matrix, or produce a fiber matrix by using the squeezer equipment.

11. The method claim 10, the film matrix is formed by casting the degassed mixture of polysaccharide and protein solution into a mold and allows drying under oven at 20 ℃ to 45℃ to yield a film.

12. The method claim 10, the porosity matrix is formed by casting the degassed mixture of polysaccharide and protein solution into a mold in a refrigerator at -30℃ to -100℃ and allows to vacuum dry under freeze-dry drying to yield a porous structure, the porosity of matrix is in the form of a pore morphology with the interconnectivity structure.

13. The method claim 10, the powder matrix is formed by dropping the degassed mixture of polysaccharide and protein solution into the freezing solution at -30℃ to -100℃ with a moderate size of the syringe, and allows to vacuum dry under freeze-dry drying to yield a powder matrix.

14. The method claim 10, the fiber matrix is formed by squeezing the degassed mixture of polysaccharide and protein solution into the coagulant of organic solvent with the squeezer apparatus, and allows drying to yield a fibrous HA bio-composite of 50um-1mm thickness.

15. The method claim 14, wherein said coagulant solution comprises water and organic solvent ; the organic solvent is chosen from the group consisting of 1,4-dioxane, chloroform, methylene chloride, N, N-dimethylformamide, N, N-dimethylacetamide, ethyl acetate, acetone, methyl ethyl ketone, methanol, ethanol, propanol, isopropanol, butanol and the mixture of each organic solvent ; the weight fraction of organic solvent

in the coagulant solution is in a range between 60% and 100%.

16. The method claim 15, wherein the ketones and alcohol can be mixed with any ratio, and the preferred weight fraction of organic solvent is in a range between 75% and 100%.

17. The method claim 1, wherein said step （c）the cross-linking agent is a carbodiimide.

18. The method claim 17, wherein said the carbodiimide is selected from the group consisting of 1-methyl-3- (3-dimethylaminopropyl)-carbodiimide, 3-(3- dimethylaminopropyl)-3-ethyl- carbodiimide, 1-ethyl-3- (3- dimethylaminopropyl)- carbodiimide and the mixture of each group.

19. The method claim 1, wherein said step （c）the water/organic solution contains 5%-50% water of ethanol or acetone solution ; adjust the pH of mixture solution to 4-5.5,the weight percent of carbodiimide is 0.5%-25% ; the temperature of reaction is 20℃-45℃,the reaction time is 1-6hrs.

20. The method claim 19, wherein said the water/organic solution contains 5%-30% water of ethanol or acetone solution ; adjust the pH of mixture solution to 4-5.5,the weight percent of carbodiimide is 1%-5% ; the reaction time is 2-4hrs.

21. The method claim 1, wherein said step （c）the cross-linked of water-insoluble polysaccharides can be washed with water/organic solution, and washing with distilled water after immersing in the salt solution.

22. The method claim 21, wherein said the water/organic solution contains 5%-50% water of ethanol or acetone solution, the immersion time is 0.5-3hrs.

23. The method claim 22, wherein said the water/organic solution contains 5%-30% water of ethanol or acetone solution.

24. The method claim 21, wherein said the salt solution is chosen from the group consisting of sodium chloride, dibasic sodium phosphate and the mixture of both, the concentration of salt is 0.15-4M.